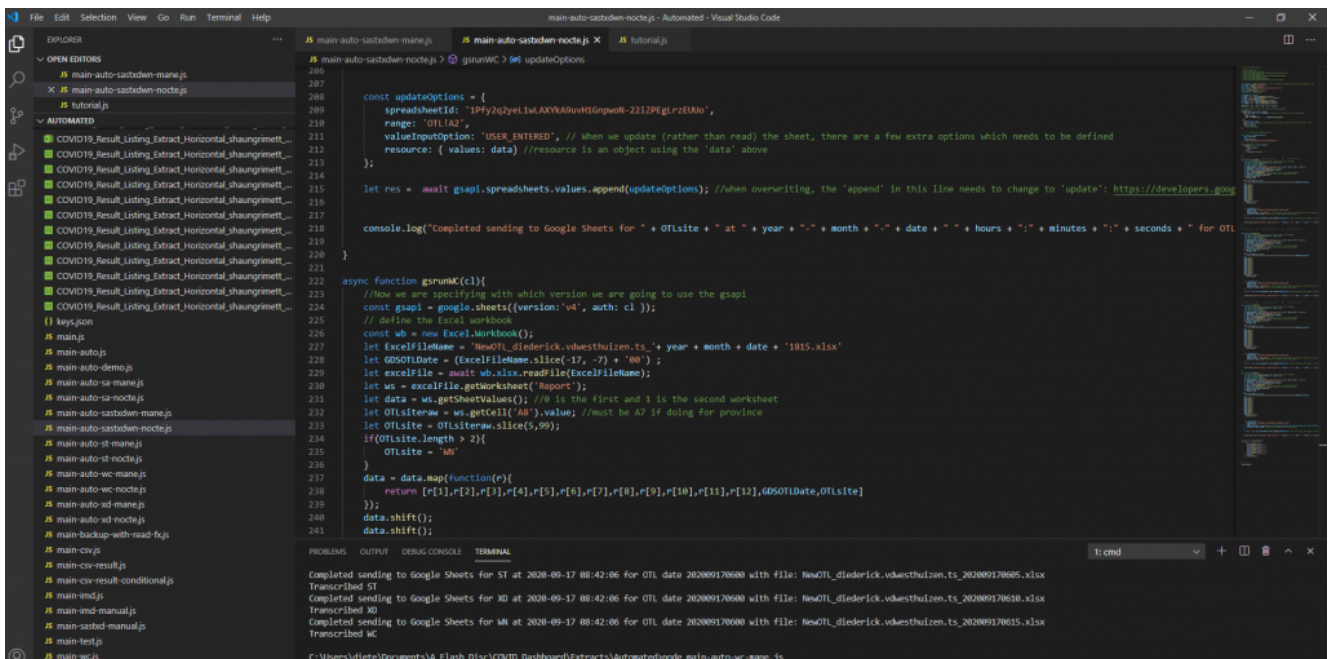


# Section 7.8 – COVID OTL Dashboard

A dashboard was created to visually represent the COVID outstanding test list for our province for COVID outstanding PCR tests. This dashboard has been requested by the area manager of the Western Cape and various others on the Virology Expert Committee. Even though not a task primarily assigned to chemical pathologists, since I have an interest in data science, I tried to help. The end result was a dashboard which is updated every morning at 06h00 and every evening at 18h00 with a few JavaScript scripts running each day, updating three databases on the backend along with automated data extractions being done from TrakCare every morning and evening at a predefined time.



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main-auto-sasbiden-node.js | gspread | updateOptions
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```
const updateOptions = {
  spreadsheetId: '1Pfy2q2ye1wAXYRA9uH5GnpwN-221ZPEgrzEUko',
  range: 'OTL!A2',
  valueInputOption: 'USER_ENTERED', // When we update (rather than read) the sheet, there are a few extra options which needs to be defined
  resource: { values: data } //resource is an object using the 'data' above
};

let res = await gsapi.spreadsheets.values.append(updateOptions); //when overwriting, the 'append' in this line needs to change to 'update': https://developers.google.com/sheets/api/reference/rest/v4/spreadsheets/values#append

console.log("Completed sending to Google Sheets for " + OTLsite + " at " + year + "-" + month + "-" + date + " " + hours + ":" + minutes + ":" + seconds + " for OTL");
}

async function gsRunK(c1){
  //Now we are specifying with which version we are going to use the gsapi
  const gsapi = google.sheets({version: 'v4', auth: c1});
  // define the Excel workbook
  const wb = new Excel.Workbook();
  let ExcelFileName = "NewOTL_diederick.vdwesthuizen.ts_" + year + month + date + ".xlsx";
  let GSOTLDate = (ExcelFileName.slice(-17, -7) + ".xlsx");
  let excelFile = await wb.xlsx.readFile(ExcelFileName);
  let ws = excelFile.getWorksheet('Report');
  let data = ws.getSheetValues(); //0 is the first and 1 is the second worksheet
  let OTLsite = ws.getCell("A2").value; //must be A2 if doing for province
  let OTLsite = OTLsite.slice(5,99);
  if(OTLsite.length > 2){
    OTLsite = 'MI'
  }
  data = data.map(function(r){
    return [r[1],r[2],r[3],r[4],r[5],r[6],r[7],r[8],r[9],r[10],r[11],r[12],GSOTLDate,OTLsite];
  });
  data.shift();
  data.shift();
}
```

```
PROBLEMS OUTPUT DEBUG CONSOLE TERMINAL
Completed sending to Google Sheets for ST at 2020-09-17 08:42:06 for OTL data 202009170600 with file: NewOTL_diederick.vdwesthuizen.ts_202009170605.xlsx
Transcribed ST
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Transcribed XD
Completed sending to Google Sheets for MR at 2020-09-17 08:42:06 for OTL data 202009170600 with file: NewOTL_diederick.vdwesthuizen.ts_202009170615.xlsx
Transcribed MR
C:\Users\dieter\Documents\Flash Disc\COVID Dashboard\Extracts\Automated\code main-auto-wc-man.js
```

Screenshot 1 – Illustration of the JavaScript code to read the extracted Excel (or CSV) files and transcribing them to a Google Sheets database.

This dashboard was used (and likely still are being used) especially by the virologists at Groote Schuur Hospital to track the progress of outstanding COVID PCR tests and it can also be used to show possible bottlenecks in pre-analytical

sample issues if tests are already registered before being sent to any of our laboratories in the Western Cape.

The dashboard consists of a few pages:

1. WC Dashboard Summary
2. Outstanding tests per OTL date
3. Outstanding tests per Registratio...
4. Outstanding tests per Location
5. Outstanding tests' details per age ...
6. WN Outstanding tests per Location
7. WN Outstanding tests per OTL date

<https://datastudio.google.com/embed/reporting/aeafe888-d10f-4959-b1f3-928556abd6f6/page/LMPXB>

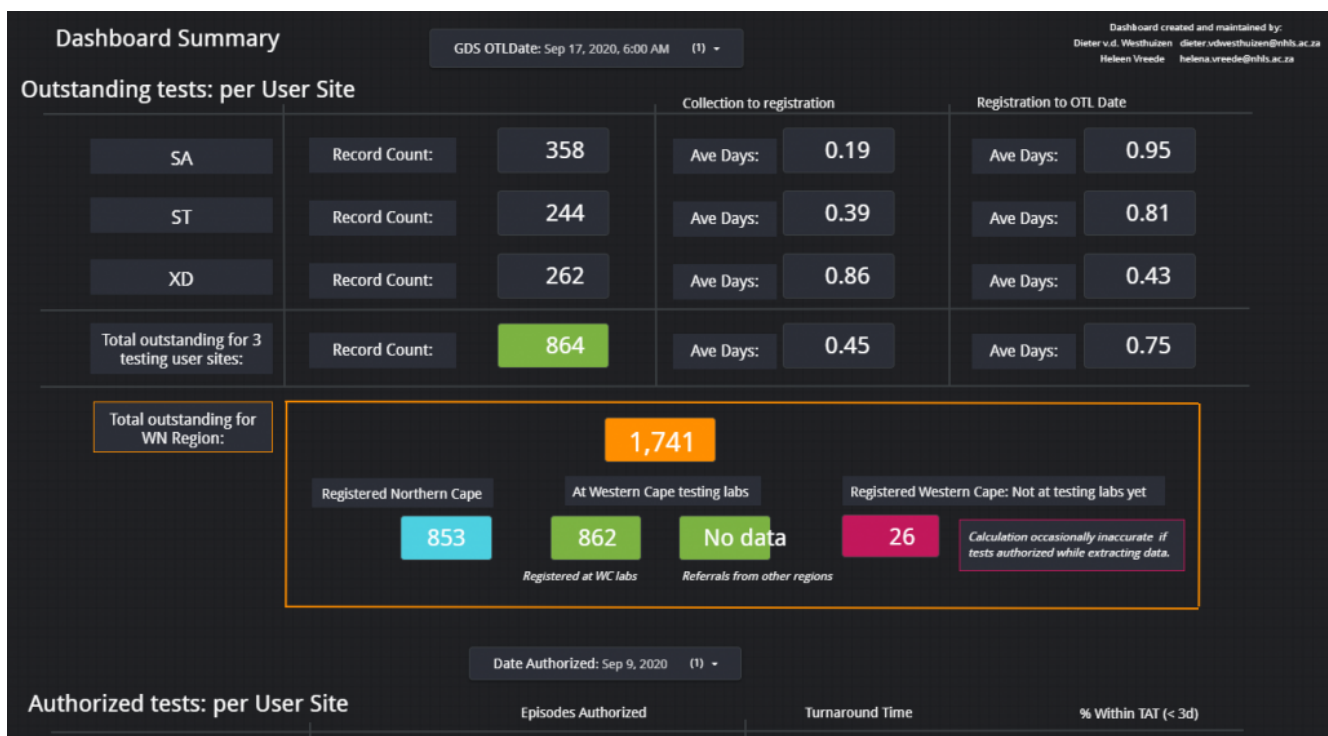


Figure 1 – Screenshot of the Dashboard. Follow the link above to view.



Figure 2 – Example of the layout of the page which shows the total count of items on the respective outstanding test lists for each respective data for the Western Cape.



Figure 3 – Outstanding tests summary by location. This page is especially helpful if the delay / outstanding tests from a specific hospital or clinic needs to be visualized in comparison with other locations (hospitals / clinics).

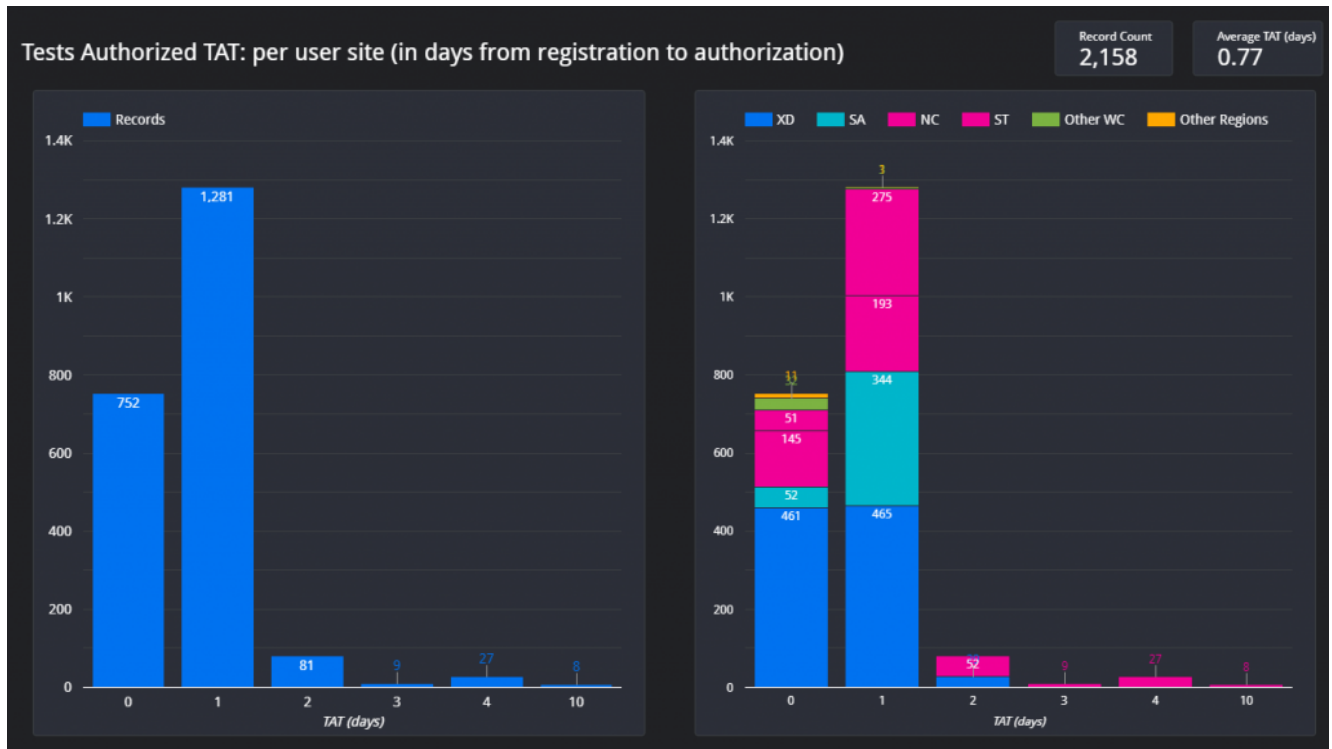


Figure 4 – Illustration of the turnaround time met by a certain count of samples per each respective user site for one day.

# Immune Responses to SARS-CoV-2 cause severe COVID-19 in some and recovery in most

Clive Gray – Professor in Immunology

[immunopaedia.org](http://immunopaedia.org) – useful web site for immunology resources.

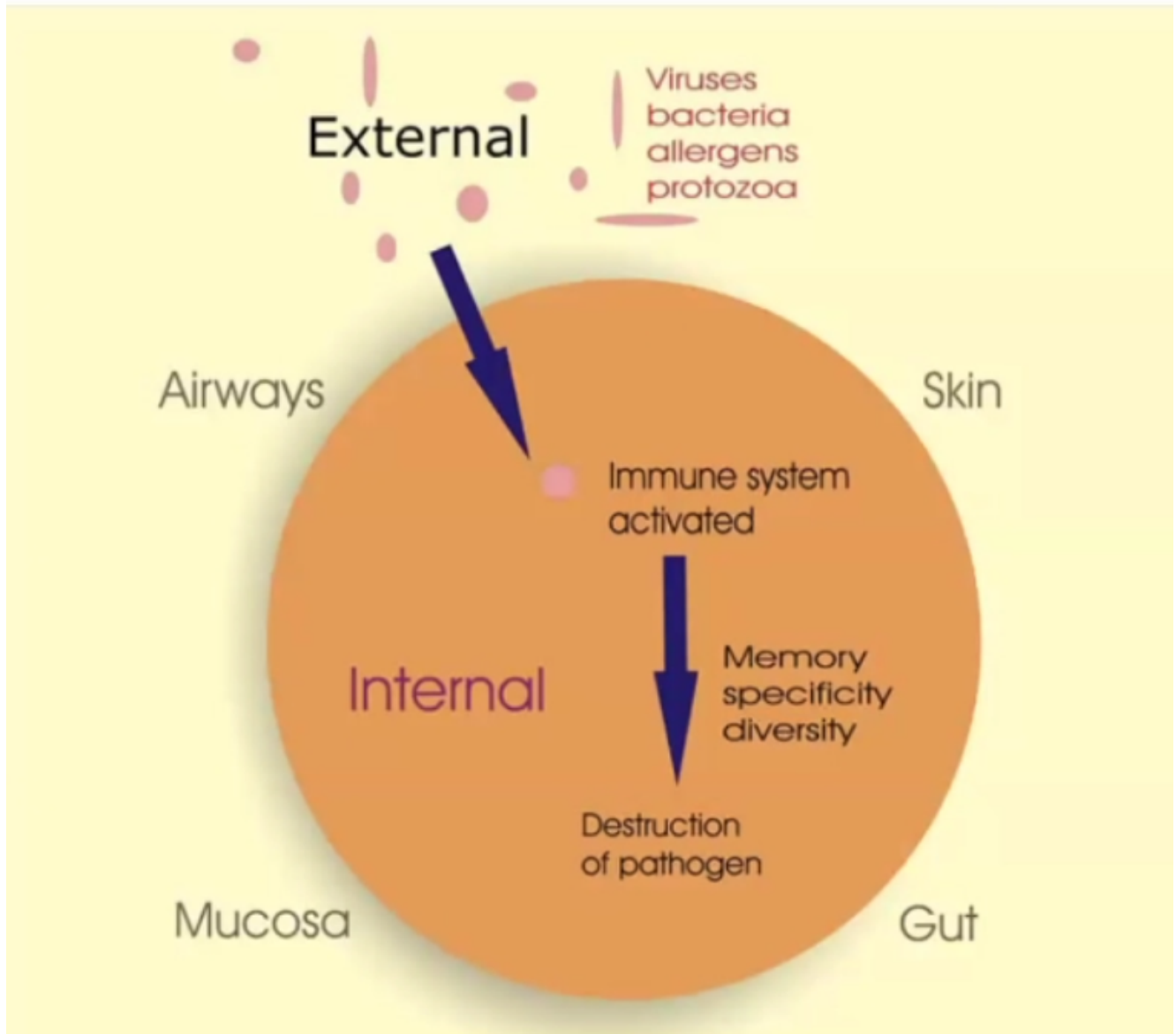
Outline:

- Basics of Immunology
- A balance between inflammation and tolerance
- What happens to people who progress to severe COVID-19?
- What might be happening in SARS-CoV-2 infected people who remain asymptomatic, have few symptoms and recover?



Internal : External world

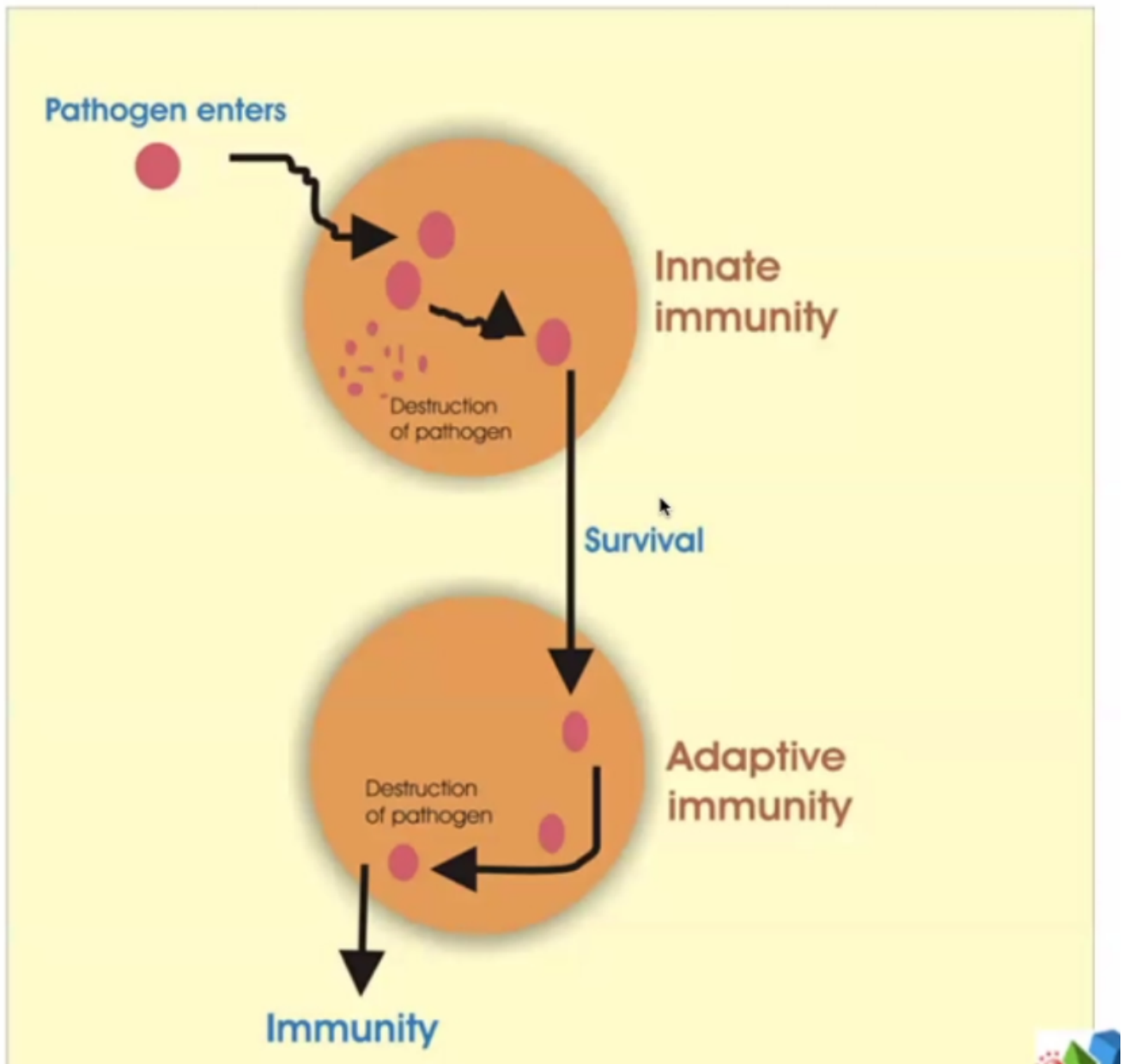
# Internal:External World



~99% of time the pathogen gets destroyed, but the pathogen may survive in rare cases.

2 arms of immune responses:

# Innate:Acquired Immunity

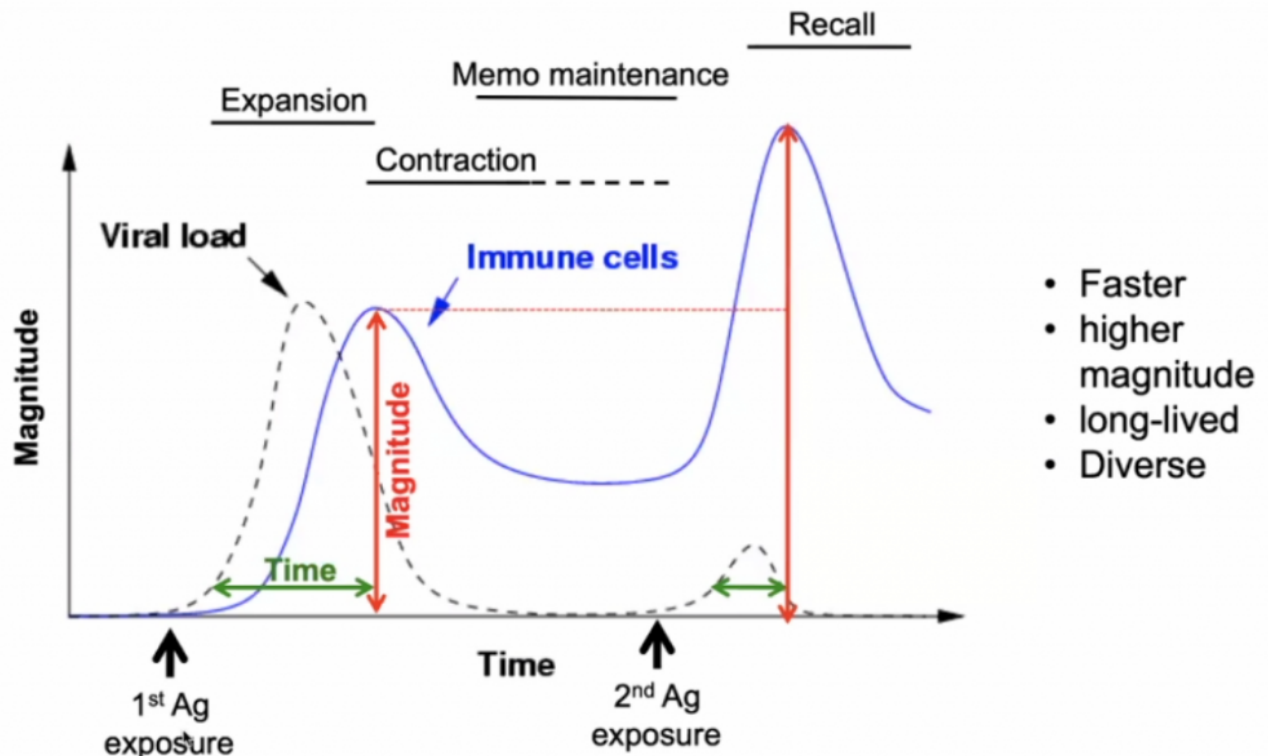


Innate – evolutionary response – very rapid – elements of innate immunity are found in bacteria, plants, lower vertebrates, squids, fish etc.

Some pathogens survive ->

Adaptive immunity – much more targeted / focussed. The immune system targets more specifically the pathogens which survive the innate immunity.

# Immune Memory is essential preserving the self

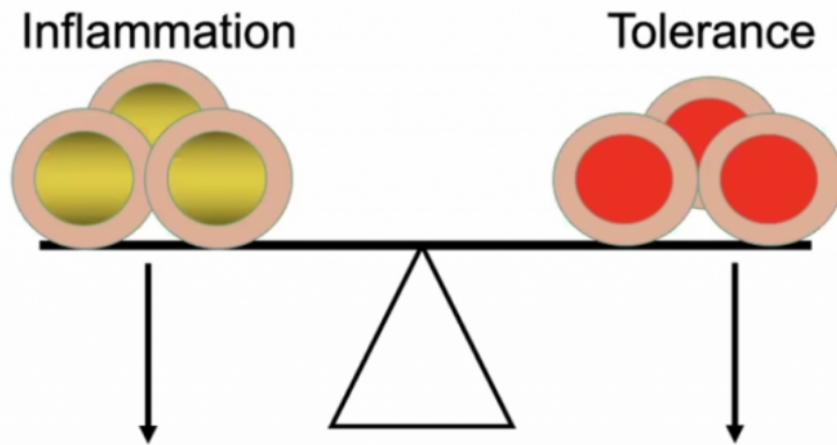


Infection initially -> expansion (peak after maximal viral load) -> contraction with some residual immunity (Memo Maintenance) -> with secondary response (Recall) there is a more rapid expansion (and higher peak) of the specific immunity.

## Immune regulation:

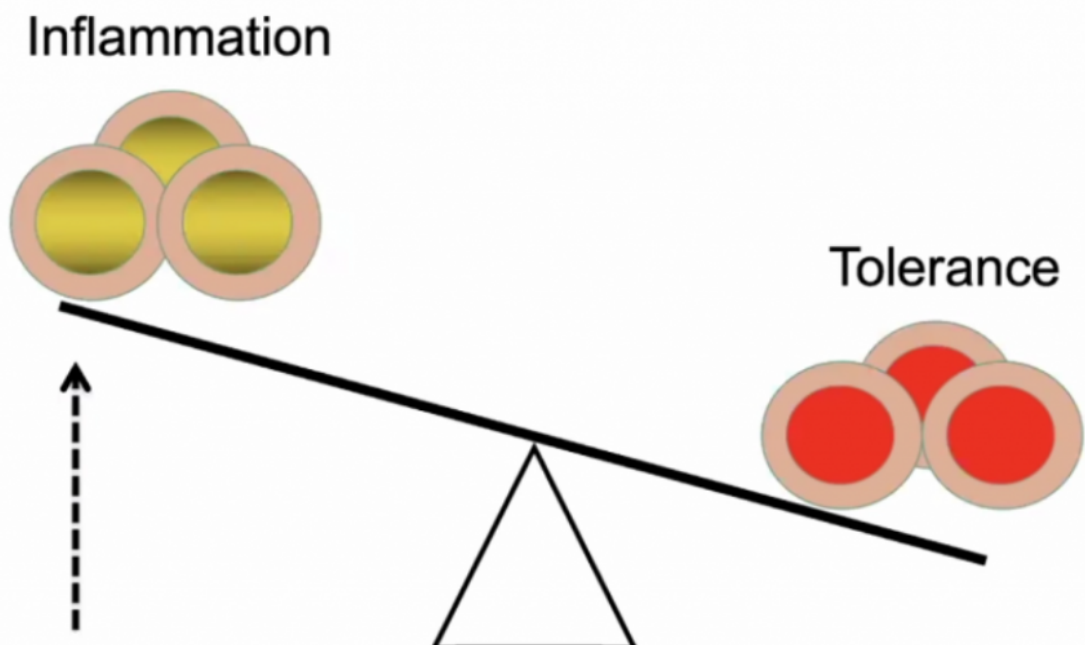
Predisposed conditions: DM, HPT, Obesity, would make an individual highly susceptible to inflammation due to imbalance of Inflammation vs. Tolerance, see below.

# The immunological equilibrium: balance between inflammation and tolerance



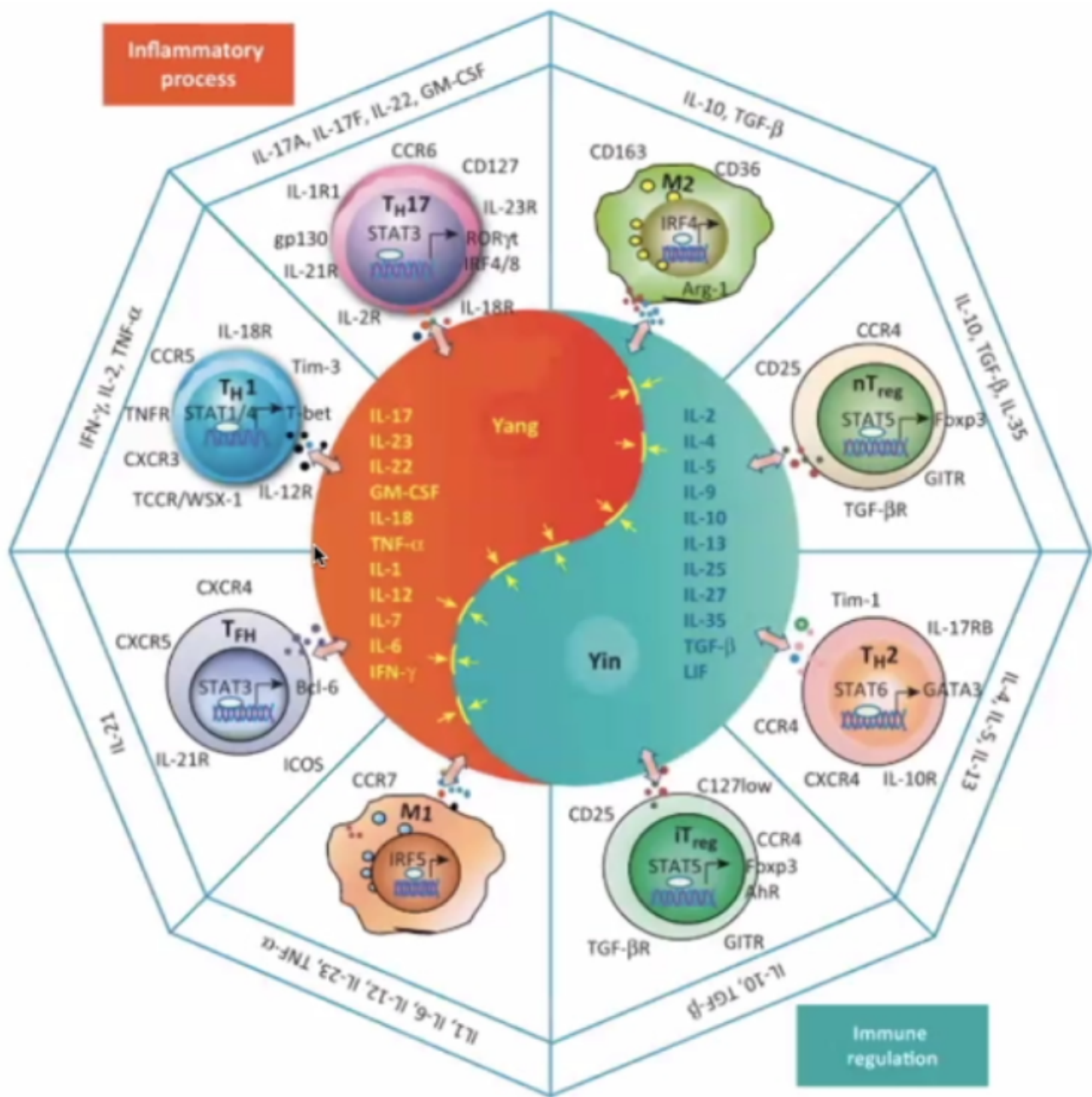
**Normal:** reactions against pathogens  
**Pathologic:** inflammatory disease, e.g. caused by reactions against self

No response to self  
Controlled response to pathogens



Pathogenic event

# The Yin Yang of immunology:



TRENDS in Immunology

Yin – immune regulation; Yang – Inflammatory Process

## Pro-inflammatory (Orange)

TH17 – inflammatory cells secreting the “calling signals” for leucocytes.

TH1 – secreting IFN gamma; IL-2 ; TNF-alpha – cytokines causing inflammation

Macrophage – presents antigens – in lymph nodes and germinal



centres

T-Helper cells T-FH

## Immune Regulation (Blue)

TH2 – hand in hand with TH1 (opposite)

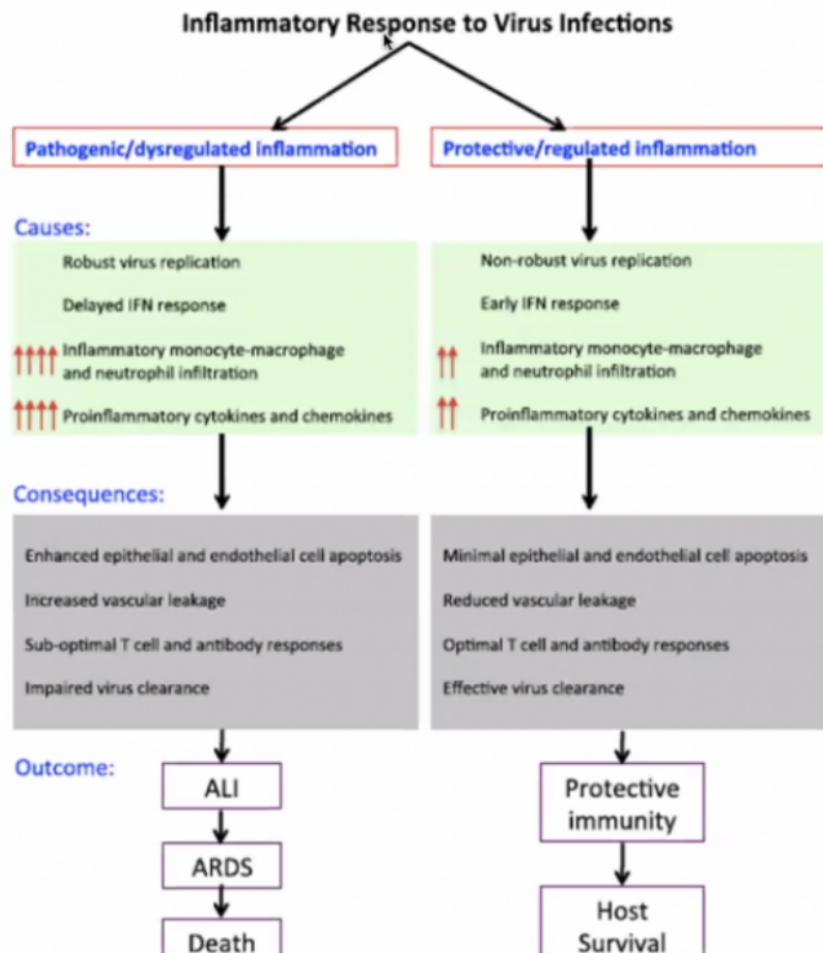
Regulatory cells (nT and iT regulatory cells)

Actual pathogen is not causing disease – but the immune response – thus this is what should be focussed on to treat the disease.

## Respiratory Infections

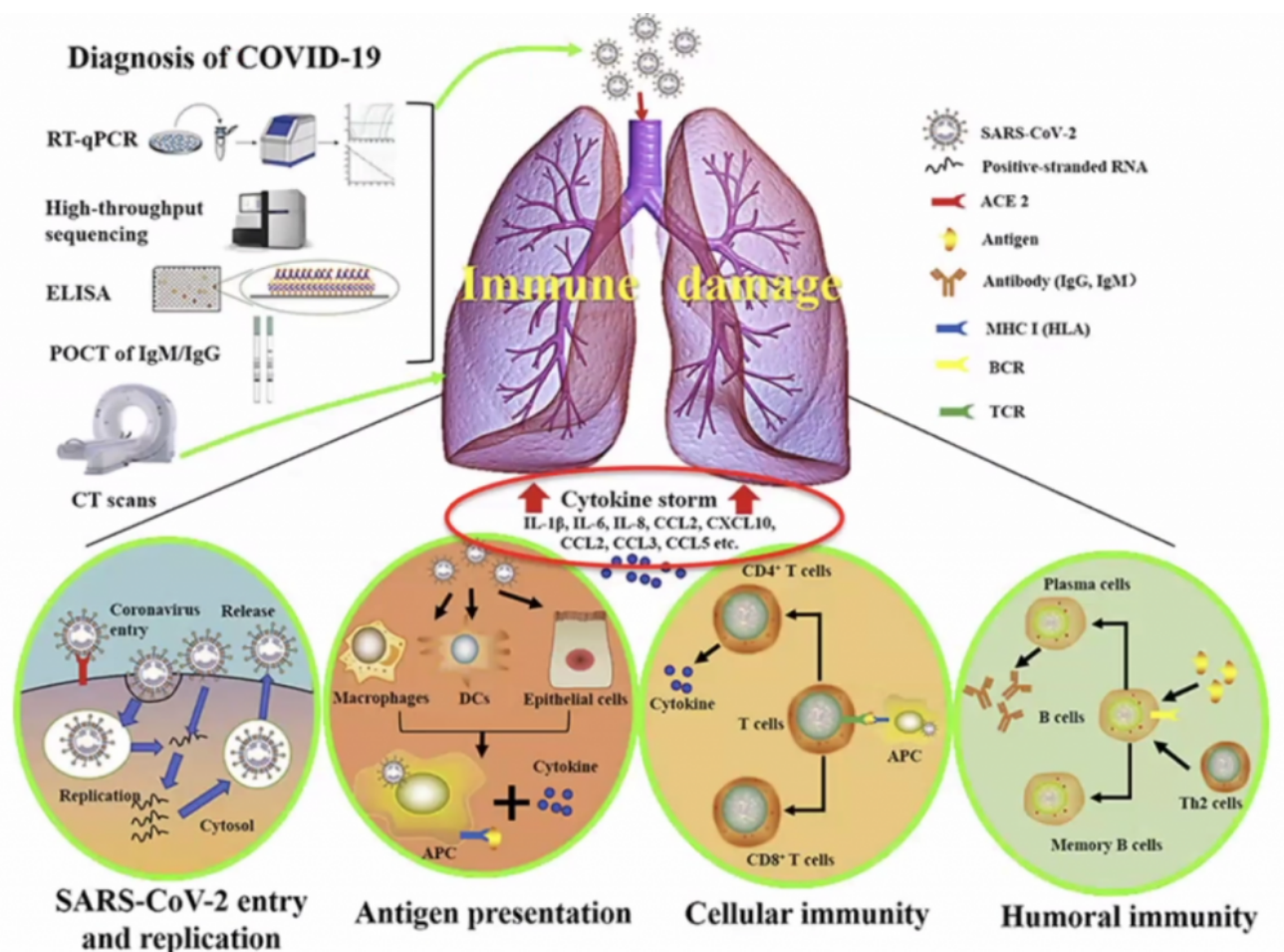
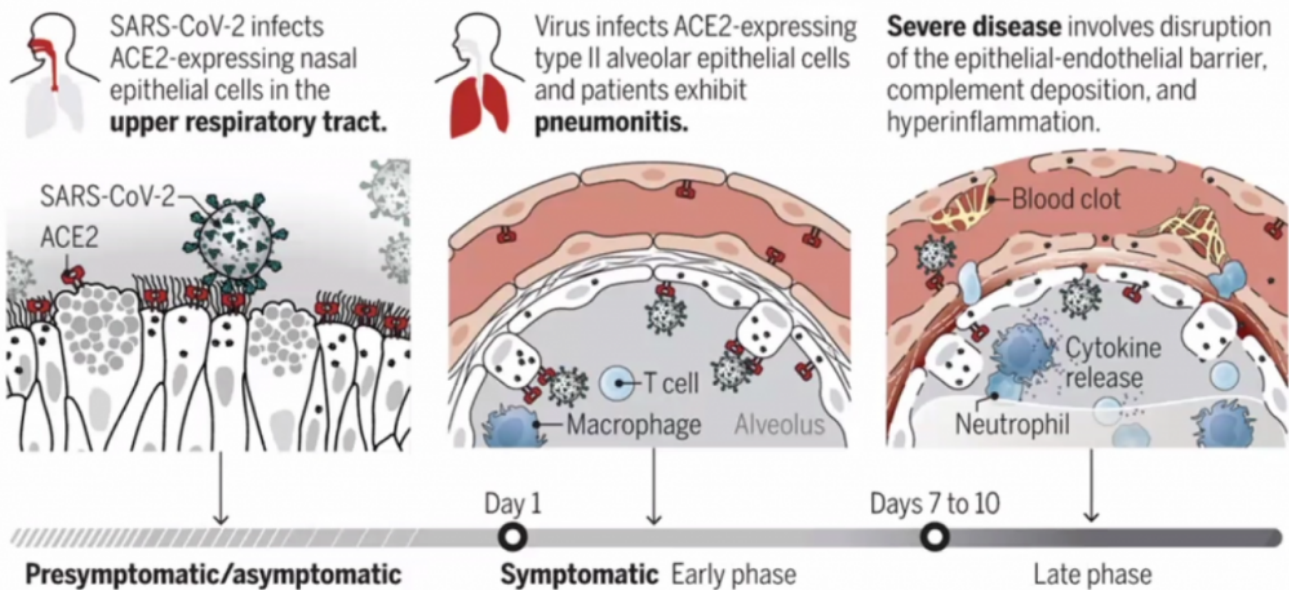
| Virus              | Entry receptor         | Common symptoms                                                                                                                                            | Clinical complications                                                                                                                                        |
|--------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Rhinovirus         | ICAM-1 or LDL          | Rhinorrhea, coryza, sneezing, sore throat, cough                                                                                                           | Asymptomatic, mild to moderate upper-respiratory tract illness, bronchitis                                                                                    |
| Common coronavirus | Strain specific        | Fever, rhinorrhea, coryza, sneezing, sore throat, cough                                                                                                    | Mild to moderate upper-respiratory tract illness                                                                                                              |
| Adenovirus         | Strain specific penton | Fever, rhinorrhea, coryza, sneezing, sore throat, cough, pink eye, diarrhea, bladder infections                                                            | Mild to moderate upper-respiratory tract illness, croup, tonsilitis                                                                                           |
| Seasonal influenza | Sialic acids           | Fever, rhinorrhea or stuffy nose, coryza, sore throat, cough, headache, myalgia                                                                            | Mild to moderate upper-respiratory tract illness, bronchitis, croup                                                                                           |
| RSV                | Nucleolin              | Fever, rhinorrhea, coryza, sore throat, cough, wheezing, shortness of breath                                                                               | Mild to moderate upper-respiratory tract illness, bronchitis, bronchiolitis, croup                                                                            |
| Enterovirus D68    | Sialic acids alpha2-6  | Rhinorrhea, sneezing, cough, mouth blisters, myalgia; wheezing and dyspnea in more severe cases                                                            | Mild to moderate upper-respiratory tract illness, bronchitis, bronchiolitis, pneumonia                                                                        |
| Pandemic influenza | Sialic acids           | Fever, coryza, rhinorrhea or stuffy nose, sore throat, cough, headache, shortness of breath, dyspnea, myalgia                                              | Bronchitis, croup, pneumonia, diffuse alveolar damage, acute respiratory distress syndrome, respiratory failure                                               |
| SARS-CoV           | ACE2                   | Fever, chills, cough, shortness of breath, dyspnea, myalgia                                                                                                | Rapidly progressive pneumonia, diffuse alveolar damage, severe acute respiratory distress syndrome, respiratory failure, fibrosis                             |
| MERS-CoV           | CD26                   | Fever, chills or rigors, coryza, sore throat, non-productive cough, sputum production, shortness of breath, dyspnea, headache, vomiting, diarrhea, myalgia | Rapidly progressive pneumonia, diffuse alveolar damage, severe acute respiratory distress syndrome, respiratory failure, septic shock and multi-organ failure |

# Protective versus pathogenic inflammatory responses to pathogenic hCoV infections



**Dose** of the virus (viral load) is key to how you respond to the virus – Initial High dose in viral load likely will lead to high inflammatory response; Low dose (non-robust virus replication) may cause a less severe inflammatory response.

# Key phases of disease progression

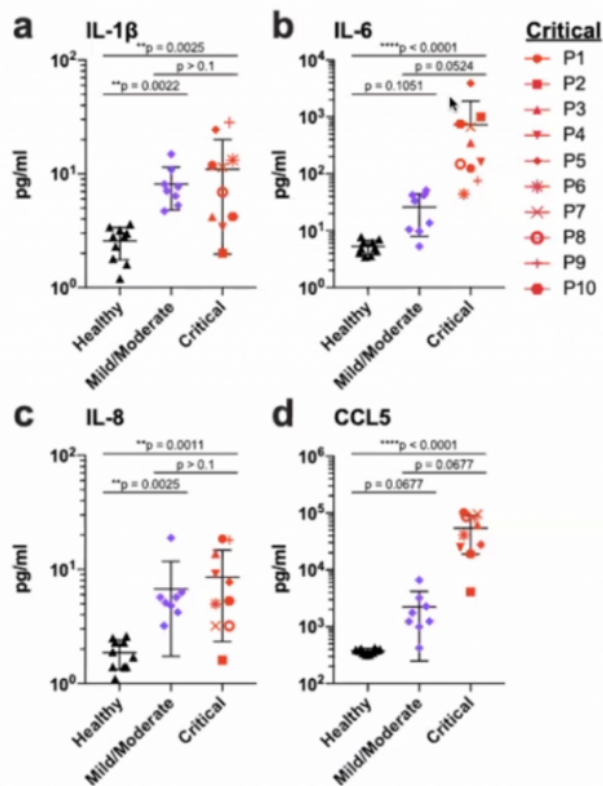


CCL's allow leucocytes to migrate, hence in a **cytokine storm**, with high level of **migration**, the leucocytes causes severe local inflammation due to migration of leucocytes to local



sites.

## CCR5 inhibitors?



When patients were treated with a [CCR5](#) blocking antibody ([leronlimab](#)), there was rapid reduction in plasma IL-6 and a significant decrease in SARS-CoV-2 plasma viremia.

Blocking CCR5 inhibits the migration of Inflammatory-inducing cells, such as monocytes and macrophages

CCL5 blocking antibodies leads to rapid reduction of IL-6. Dexamethasone is not so much an inhibitor of CCR5, but it prevents the hyperinflammation by inhibiting the majority of the inflammatory pathway.

# Recovery: what might be going on?

## South Africa

### Current percentage distribution of all cases



88.6% recovery  
2.36% mortality (254/10<sup>6</sup> popn)

## Global

### Current percentage distribution of all cases

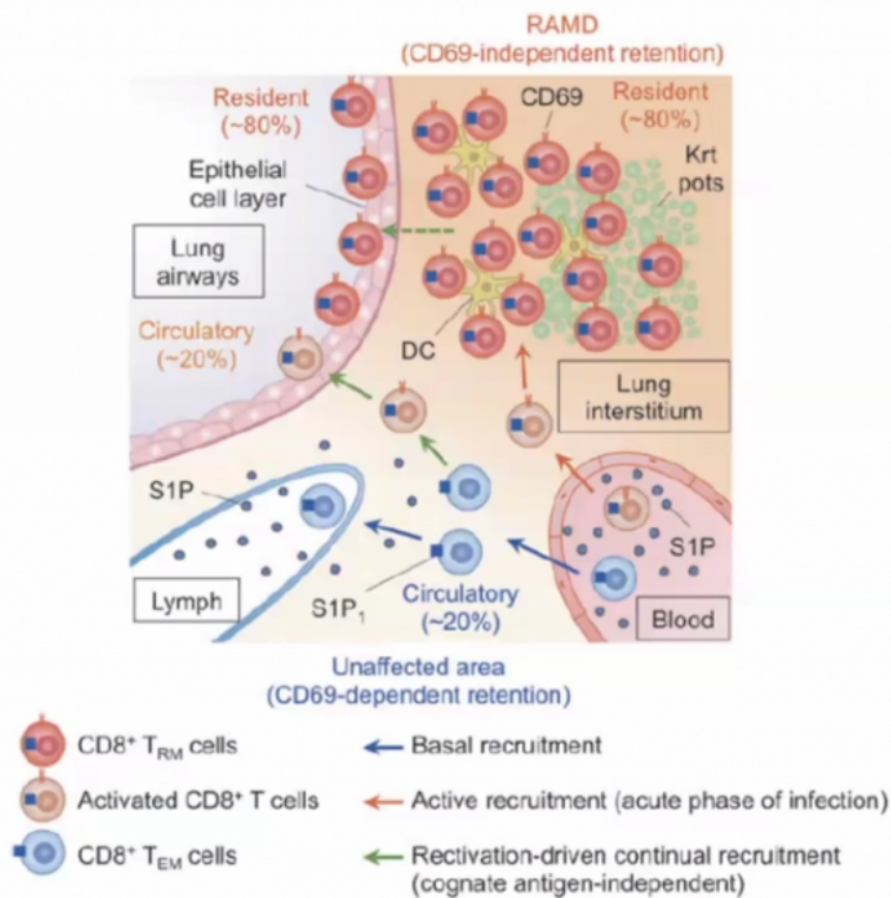


72% recovery  
3.24% mortality (116/10<sup>6</sup> popn)

CD8 cells

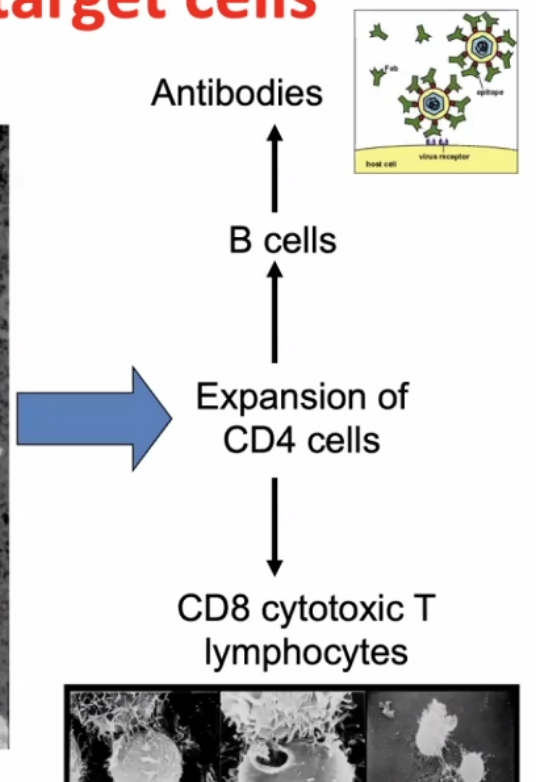
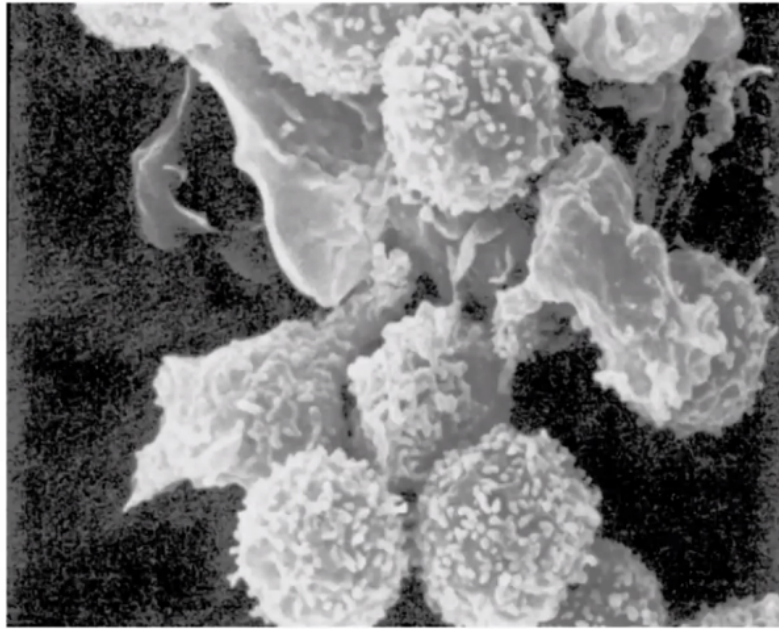


# Special CD8<sup>+</sup> cells in the lung: possible protection



Within interstisium, the CD8 cells are present and

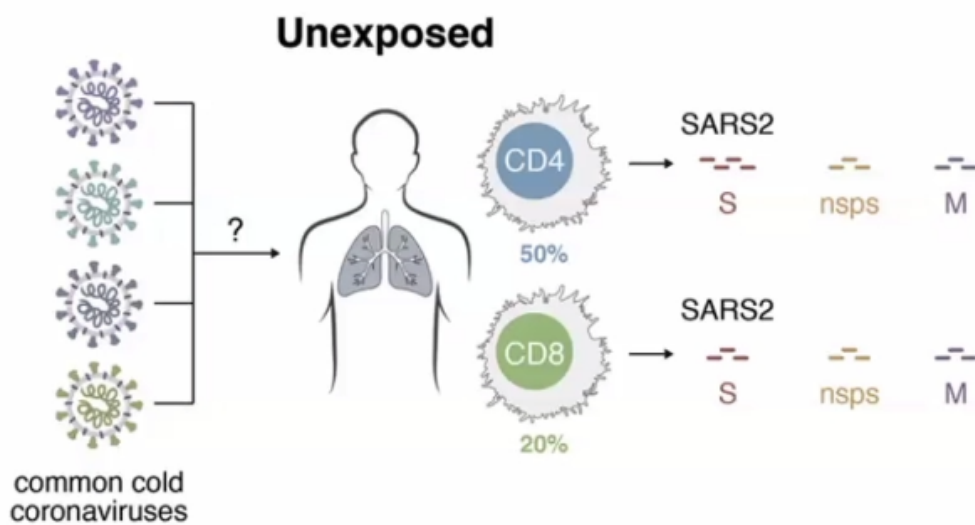
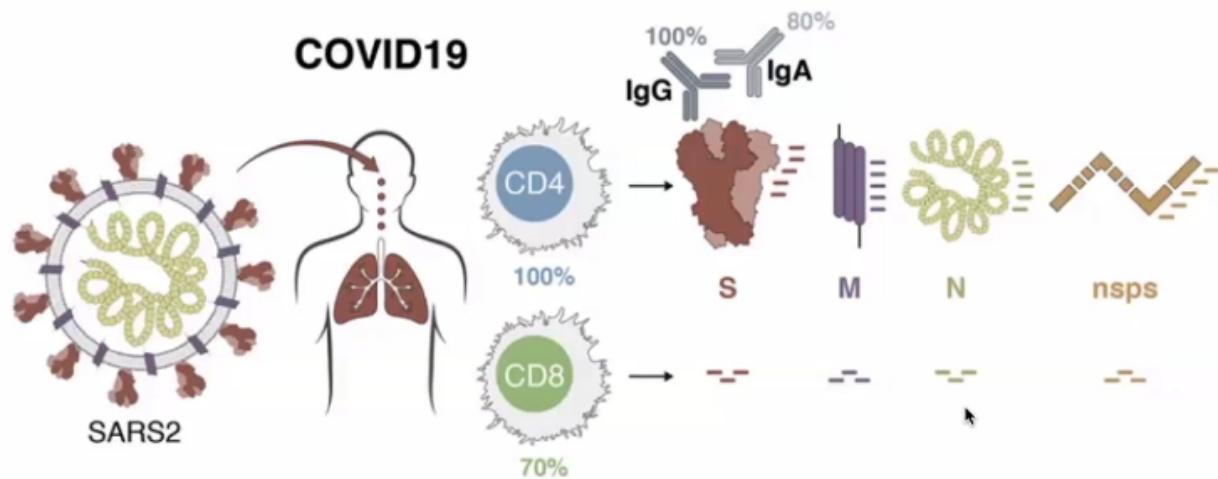
## CD4<sup>+</sup> cells help B cells makes antibody and CD8 cells kill target cells



CD4 cells activates CD8 cells, hence called T-helper cells.

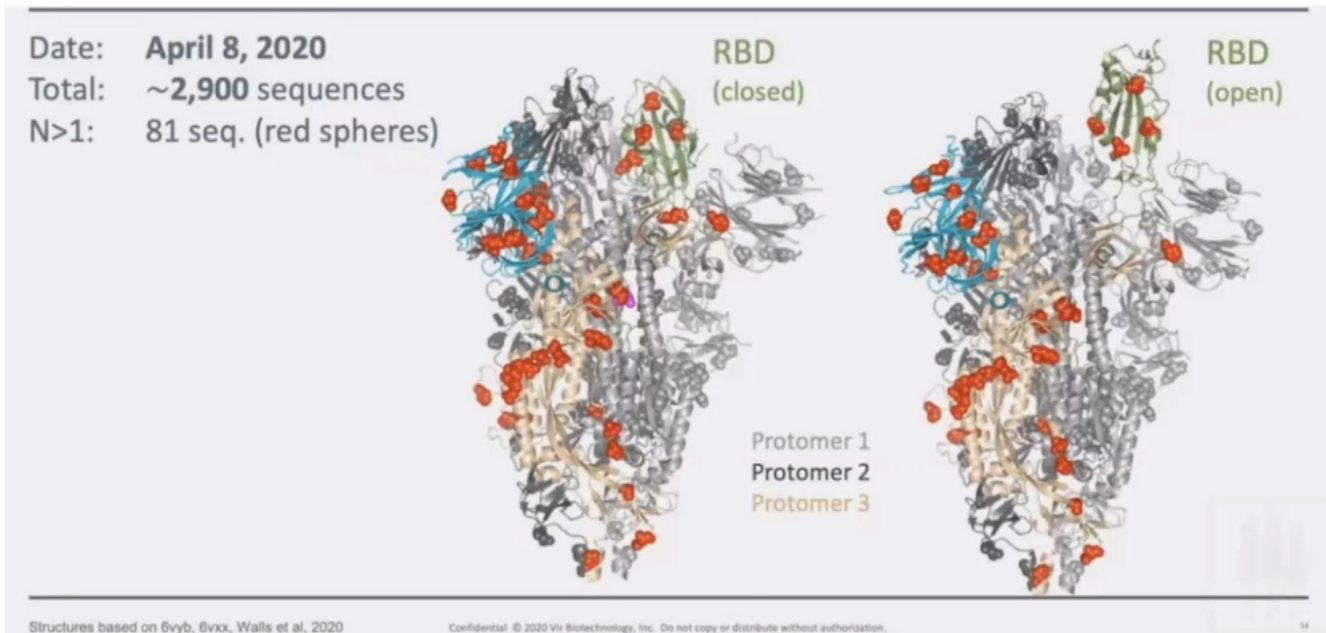
## Is there Evidence for pre-existing immunity?

- Preexisting T cell immunity existed to H1N1 in the adult population ([Greenbaum et al 2009](#))
- The presence of cross-reactive T cells was found to correlate with less severe disease ([Sridhar et al 2013](#); [Wilkinson et al 2012](#))
- Substantial cross-reactive coronavirus T cell memory has been observed ([Grifoni et al 2020](#))

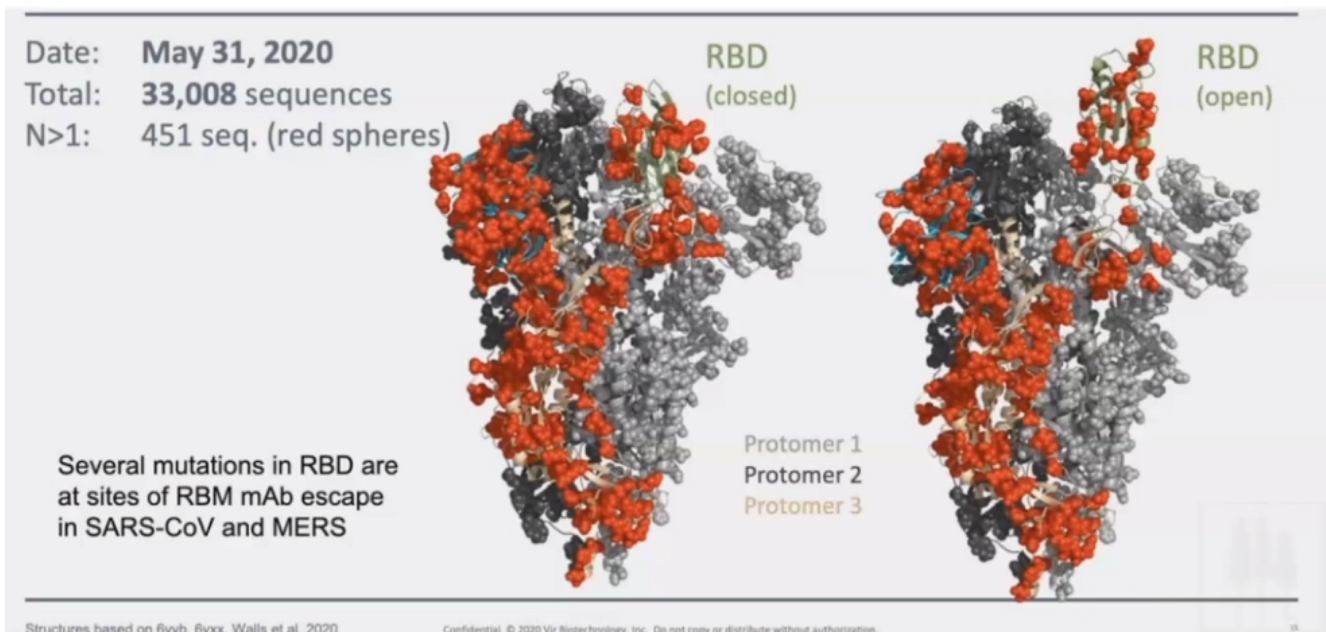


T-cell responses are very prevalent to COVID-19 exposed individuals. BUT CD4 cells and CD8 cells can also react to the SARS2 viral proteins in unexposed individuals.

# Rapid Evolution of SARS-CoV-2



RBD – receptor binding domain (Spike-protein); Orange is the amount of amino acids which are changeable.



Orange amino acids are those which are changeable – illustrating how the virus has mutated in a month.



# Conclusions

- Hyperinflammation involving chemokines and inflammatory innate and adaptive immune cells migrate to “hot” areas of damage (lung, heart, GIT etc)
  - Key to treatment is to either dampen inflammation or to block the migration of inflammatory cells to the lungs
  - The majority of infected people recover. Is this due to some form of pre-existing immunity?
  - Evidence suggest this may be the case.
- 

## Section 7.1 – Publications by Candidate

*COVID-19 Related Laboratory Analyte Changes and the Relationship between SARS-CoV-2 and HIV, TB and HbA1c in South Africa*

*Reinhardt Hesse, Dieter van der Westhuizen, Jaya George*

We conducted a retrospective analysis on data of all adults tested for SARS-CoV-2 across our laboratory network in South Africa over a 4-month period. Out of 842,197 tests 11.7% were positive and 88.3% negative. The prevalence of HIV was 6.25 and 6.31% in the SARS-CoV-2 positive and negative cohort

respectively ( $p=0.444$ ). However, the prevalence of HIV positive individuals in the critical cohort (9.15%) was higher than in the non-critical group (6.24%) ( $p=0.011$ ). Active tuberculosis infection was approximately 50% less in SARS-CoV-2 positive than in negative individuals. The prevalence of uncontrolled diabetes was 3.4 times higher in SARS-CoV-2 positive cases, but was not higher in the critical vs. non-critical cases ( $p=0.612$ ). The neutrophil-to-lymphocyte-ratio, coagulation markers, urea, cardiac, and liver related analytes were significantly elevated in the critical compared to non-critical cases. Platelet count and creatinine concentration did not differ significantly between the two groups. These findings do not support increased prevalence of HIV or tuberculosis in individuals with SARS-CoV-2 infection but do suggest an association of increased disease severity with HIV positive status. Uncontrolled diabetes was positively associated with a significantly higher prevalence of SARS-CoV-2 and our investigation into analyte changes associated with SARS-CoV-2 disease severity supported previous findings of raised inflammatory markers, coagulation markers, liver and cardiac related analytes and urea, but not for creatinine and platelet count.

See the full article (book chapter) below:

[https://www.researchgate.net/publication/343650512\\_COVID-19\\_Related\\_Laboratory\\_Analyte\\_Changes\\_and\\_the\\_Relationship\\_between\\_SARS-CoV-2\\_and\\_HIV\\_TB\\_and\\_HbA1c\\_in\\_South\\_Africa](https://www.researchgate.net/publication/343650512_COVID-19_Related_Laboratory_Analyte_Changes_and_the_Relationship_between_SARS-CoV-2_and_HIV_TB_and_HbA1c_in_South_Africa)

*Acute Kidney Injury during the COVID-19 Pandemic – Experience from Two Tertiary Centres in South Africa*

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**Background:** The first case of SARS-CoV-2 in South Africa [SA] was documented in March 2020. By October, the total cases for the Western Cape and Gauteng Provinces were 331,425 with 8456 fatalities. The aim of this study was to describe the prevalence of acute kidney injury [AKI] in hospitalized patients with COVID-19 in two tertiary centres in SA. **Methods:** SARS-CoV-2 positive patients admitted to two tertiary centres in SA between 18 March and 31 August 2020 were included in the study. Demographic data, pre-existing comorbidities, admission variables, laboratory data, management and hospital outcomes were captured. Exclusion criteria included age <18 years, pre-existing Stage 4 or 5 chronic kidney disease and prior renal transplant. Outcomes assessed were the need for acute dialysis, recovery from AKI, discharge and death. **Results:** AKI occurred in 374/1102 (33.9%) patients admitted to the two hospitals. Within the AKI cohort, 91 (24.3%) patients required intensive care unit [ICU] management, and 32 (8.6%) received kidney replacement therapy. Older age ( $P = 0.001$ ), pre-existing hypertension [HPT] ( $P = <0.0001$ ) and biochemical evidence of severe disease, including high ferritin, lactate dehydrogenase, d-dimer and C-reactive protein, were significantly higher in the patients with AKI versus those without. AKI Stage 3 had a higher mortality and lower rates of renal recovery upon discharge. AKI was significantly associated with an increased utilization of ICU resources, prolonged length of stay and mortality. **Conclusion:** This study reports the largest cohort of COVID-19-associated AKI in Africa. Older age, HPT and severe COVID-19 infection were significantly higher in patients with COVID-19 who developed AKI. This cohort had high rates of AKI which was associated with adverse outcomes, including mortality.

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